veracity for the public and for health officials. Alternatively, failure to adequately address these domains may erode of the public’s trust in public health recommendations.

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References


“Original antigenic sin”: A potential threat beyond the development of booster vaccination against novel SARS-CoV-2 variants

Maryam Noori MD1, Seyed Aria Nejadghaderi MD2,3 and Nima Rezaei MD, PhD4,5,6

1Student Research Committee, School of Medicine, Iran University of Medical Sciences, Tehran, Iran, 2Systematic Review and Meta-analysis Expert Group (SRMEG), Universal Scientific Education and Research Network (USERN), Tehran, Iran, 3School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran, 4Research Center for Immunodeficiencies, Children’s Medical Center, Tehran University of Medical Sciences, Tehran, Iran, 5Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran and 6Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA), Universal Scientific Education and Research Network (USERN), Tehran, Iran

To the Editor—Recently, concern has increased over the emergence of novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants, which are spreading rapidly across the globe. These variants of concern (B.1.1.7, B.1.351, P.1, and B.1.427/429) have been initially reported in the United Kingdom, South Africa, Brazil, and California, respectively. All of the currently available vaccines that have received emergency use authorization, such as Johnson & Johnson, Moderna, and Pfizer/BioNTech, are based on the Wuhan-originated virus.

Regarding the novel variants, the accumulation of multiple mutations in the spike protein, which is the target for neutralizing antibodies, has challenged the efficacy of these vaccines. Several previous laboratory-based studies have reported that the neutralizing activity of sera obtained from individuals who were vaccinated is lower against novel SARS-CoV-2 variants, highlighting the need for developing a booster vaccination containing new mutations of the virus.

A phenomenon called “original antigenic sin” (OAS) was firstly proposed by Francis in 1960. This phenomenon occurs in the second exposure of the immune system to a similar pathogen to which it has previously been exposed. In this situation, the immune system progresses to the memory response, generating cross-reactive antibodies that may not be effective against the new pathogen. In addition, it has been speculated that overproduction

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of memory B cells could compromise the activation of naive B cells capable of producing efficient and novel antibodies. In this way, OAS can trigger immune evasion of the emerging variants in those who had been infected by or vaccinated against former versions of the pathogen. In the context of coronaviruses, cross-neutralization is a rare event, but cross-reactivity in antibody binding to spike protein is common in SARS-CoV-2 and SARS-CoV. Furthermore, some degrees of cross-reactivity have also been demonstrated between seasonal coronaviruses and SARS-CoV-2. Aydillo et al11 reported a strong back-boosting of antibodies in SARS-CoV-2–infected patients previously infected with human β-coronaviruses. Interestingly, a negative correlation was observed between pre-exposure to human β-coronaviruses and induction of antibodies against SARS-CoV-2, mentioning the reduction of de novo humoral immune response and occurrence of OAS in patients with pre-existing immunity against related coronaviruses.11

The impact of OAS in developing vaccines is of paramount interest. The hypothesis of antigenic distance was proposed to explain how the efficacy of vaccines could be influenced by the difference or relatedness of prior vaccinations. This hypothesis is substantially evident in the case of dengue fever–related vaccine research. Once an individual is immunized against a dengue virus variant, the booster shot for the second variant is unlikely to be successful because it triggers only the original neutralizing antibodies rather than effective antibodies for the new variant.12 This scenario also applied to the human papillomavirus Gardasil 9 vaccine. The vaccine contained 4 antigens presented in the original Gardasil in addition to 5 novel antigens. Individuals who had been vaccinated previously by original Gardasil exhibited lower levels of antibodies against 5 new antigens compared with those who had been never vaccinated for human papillomavirus.13 In the context of influenza infection, Choi et al14 noticed that who had been never vaccinated for human papillomavirus. 13 levels of antibodies against 5 new antigens compared with those been vaccinated previously by original Gardasil exhibited lower

This trial has been designed in 2 arms. The first arm evaluates the administration who have received 2 vaccinations of mRNA-1273, the trial has been designed in 2 arms. The first arm evaluates the administration of a booster dose containing mRNA-1273.351 solely, whereas the second arm contains both mRNA-1273.351 and mRNA-1273 in equal proportions. The consequences of this trial could shed light on how OAS may alter the effectiveness of booster vaccination for novel SARS-CoV-2 variants. Eventually, further well-designed animal or human studies on a different type of vaccines are required to evaluate the efficacy of booster immunization over the potential threat of OAS in SARS-CoV-2 vaccines.

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References


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